Physiological Foundations Spring 2005: Midterm Examination

March 9, 2005

Name: _____

SSN: _____

I certify that all of the work in this exam is entirely my own. I have not referred to any notes or to any other individual while taking this exam.

Signature: _____

1. a)_____/2

   b)_____/1

2. _____/2

3. a)_____/3

   b)_____/3

4. _____/5

5. a)_____/3

   b)_____/3

   c)_____/3

   d)_____/3

6. a)_____/4

   b)_____/6

7. a)_____/4

   b)_____/4

8. _____/5

9. _____/5

10. a)_____/4

    b)_____/4

    c)_____/4

11. _____/4

12. _____/4

13. _____/4

14. _____/4

15. _____/4

16. _____/4

17. _____/4

18. _____/4

Total _____/100

Question 1 (3 Points)

There is a location in the brain that is critical for production of language. This location is in one of the cerebral hemispheres drawn below.

Part a) (2 Points) Draw the location in one of the hemispheres (it is important that you pick the correct hemisphere).

Frontal lobe

Parietal lobe

Left hemisphere

Right hemisphere

Temporal lobe
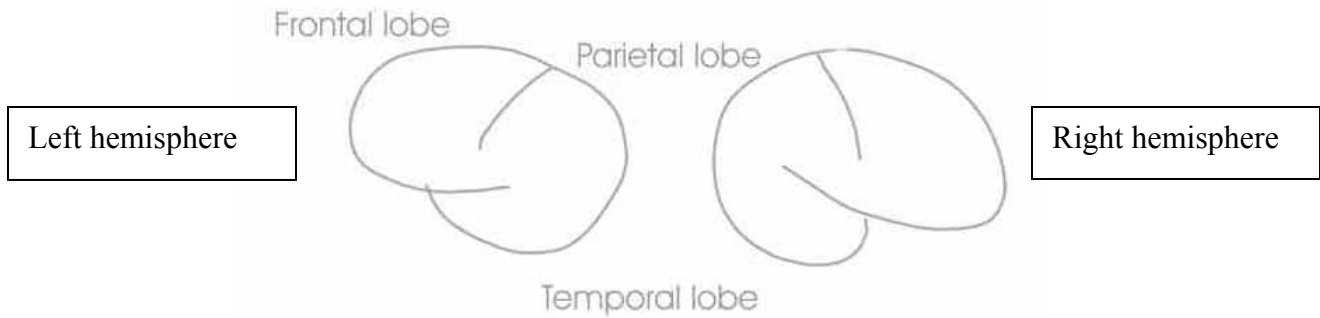
Part b) (1 Points) Indicate the name of this region.

Question 2 (2 Points)

Give one important function of glia cells.

Question 3 (6 Points)

Part a) (3 Points) The drawing below shows part of the circuitry of the cerebellum. Label the seven cells shown as *interneurons (I)* or *principal cells (P)*. In doing this part, treat the cell marked "CN" as a <u>separate nucleus</u> from the other cells. The triangles show synaptic contacts, the lines show axons, and the shaded structures are neurons. In addition to the triangles, there is a synaptic connection from *mf* to both *GC* and *G*. Label the neurons on this sheet.

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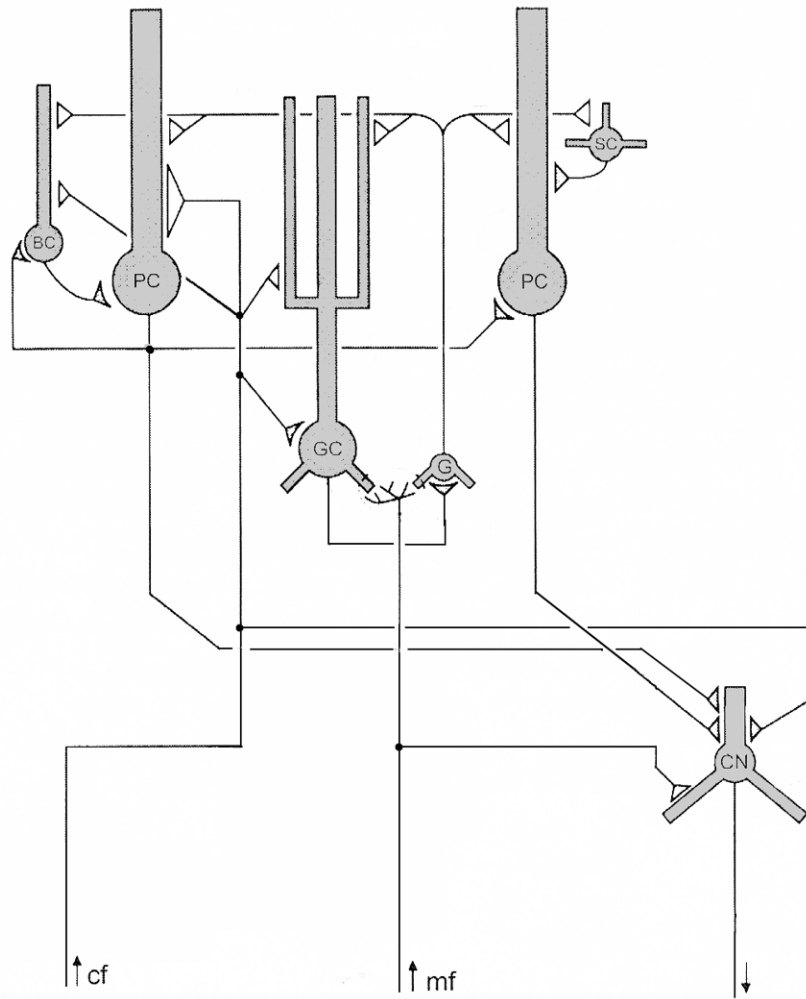
Part b) (3 Points) Identify at least two <u>feedforward interneuronal pathways</u> and one <u>feedback interneuronal pathway</u>. Give the answer as a sequence of neural elements starting from one of the inputs (*cf* or *mf*) and ending on one of the principal cells OR starting with one of the principal cells and ending on a principal cell. Thus mf→PC→SC would be a (wrong!) possible answer. Your answers must contain at least three elements, so that mf→CN is not a correct answer.

Question 4 (5 Points)

In a new species, a barium-selective channel is found in certain cells. The concentration of barium inside the cells is 1.3 mM and outside the cells is 0.1 mM. When the channel is activated, does it hyperpolarize or depolarize the cell (the cell's resting potential is –52 mV)?

Question 5 (12 Points)

Some multiple choice questions:

Part a) (3 Points) The action potential in squid giant axon is terminated by _____.

1) Sodium-channel inactivation
2) Potassium-channel activation.
3) Chloride channel activation.
4) 1) and 2) together.

Part b) (3 Points) A potassium channel like the A-channel that contains both activation and inactivation gates _____.

1) Can delay the onset of spiking if depolarization is preceded by hyperpolarization.
2) Cannot possibly affect the resting potential because of its inactivation gate being closed.
3) Only conducts current at the end of a depolarization.
4) Can cause action potentials to fire faster, like a sodium channel, which also has an inactivation gate.

Part c) (3 Points) Calcium ions are <u>removed</u> from the cytoplasm by _____.

1) Calcium channels
2) ATP-dependent active transport.
3) SERCA pumps into the endoplasmic reticulum.
4) All the above.
5) (1) and (2) above.
6) (2) and (3) above.

Part d) (3 Points) In response to activation of an <u>ionotropic</u> synapse, one observes an inward current lasting ≈1 ms followed by an outward current lasting several ms. This behavior could occur due to _____.

1) Sodium current flowing through the synaptic channel, followed by calcium current driven by the change in resting potential of the cell caused by accumulation of sodium in the cytoplasm.
2) Potassium current flowing through the synaptic channel, followed by sodium flowing through a potassium activated sodium channel.
3) Calcium current flowing through the synaptic channel, followed by potassium current through a calcium-gated potassium channel.
4) Activation of a G-protein which activates two ion channels with different time courses, say sodium followed by potassium.

Question 6 (10 Points)

Part a) (4 Points) What is the relationship between gating of a single ion channel of type X and gating of a whole-cell ion current consisting of channels of type X? Answer this by drawing a picture of the currents that flow in each case.

Part b) (6 Points) Write equations for models of the <u>current</u> flowing through three kinds of channel: 1) voltage-gated channel; 2) ionotropic receptor channel; 3) calcium-activated (but not voltage-gated) channel. These don't need to include the full details, with parameters, of the models, but do specify what functions need to be written down. That is, an equation of the form $I = G*h*$ . . . will not be a sufficient and complete answer, by itself.

Question 7 (8 Points)

Part a) (4 points) List the steps in synaptic transmission.

Part b) (4 Points) Some psychoactive drugs are blockers of molecules that transport neurotransmitters across the cell membrane, from the extracellular to the intracellular space. Explain how such a drug would change neurotransmission. Would it make the synapse stronger or weaker, for example?

Question 8 (5 Points)

In lecture, the transduction cascade in olfactory receptor neurons was described. cAMP second messenger is produced by membrane olfactory receptors through a G-protein. A channel is gated on by cAMP, admitting Na^+ and Ca^{++} to the cytoplasm, depolarizing the cell. The rise in intracellular Ca^{++} opens a Ca-gated Cl^- channel, which amplifies the depolarization. This caused confusion on the part of the lecturer, because Cl^- is not expected to amplify a depolarization. Explain why Cl^- current would ordinarily not depolarize the cell and explain how a Cl^- current could be made depolarizing.

Question 9 (5 Points)

When glutamate is released at a synapse, it can cause immediate short-term depolarization of the postsynaptic terminal. Glutamate can also cause longer-term effects such as changing the resting potential of the cell. These effects have different pharmacology, i.e. are blocked or facilitated by different substances. Explain how one neurotransmitter can have such different effects.

Question 10 (12 Points)

Part a) (4 Points) An unmyelinated axon is voltage clamped at one end, hyperpolarizing the membrane potential by 10 mV. In the steady state (i.e. when $dV/dt = 0$), write an equation for the membrane potential of the axon. ASSUME that the axon is very long, so that it can be assumed to be infinite.

Part b) (4 Points) Suppose the axon is 4 μm (4×10^{-6} m) in radius and has parameters $R_m = 10^4$ Ωcm^2, $R_i = 200$ Ωcm, and $C_m = 1$ μFd/cm^2. What is the membrane potential 1 mm away from the voltage-clamped end?

Part c) (4 Points) When the experiment is done with hyperpolarization, as above, the actual potential is experimentally found to be very close to the theory. However, when the axon is <u>depolarized</u> by 10 mV, it is found that the membrane potential doesn't behave like the simple cable theory. Explain (qualitatively) why.

Question 11 (4 Points)

Suppose you want to teach a simple perceptron to learn the logical biconditional relation ("A if and only if B") as follows:

First input (x_1)	Second input (x_2)	Desired output (Y)
0	0	+1
0	1	−1
1	0	−1
1	1	+1

The actual output of the perceptron is given by
$$y = w_1 x_1 + w_2 x_2 - \theta$$
where the weights w_1 and w_2 can be adapted by gradient descent of an error function. The threshold parameter θ can be adapted similarly because it may be regarded as another weight for an imaginary constant input that always equals to −1. Suppose the output is classified according to whether $y > 0$ or $y < 0$. Can this perceptron eventually learn the desired input-output relation correctly? Briefly explain why.

Question 12 (4 Points)

Consider a multilayer perceptron shown in the diagram. Its output y depends on the inputs x_1, x_2, x_3 as well as the synaptic $w_1, w_2, \cdots, w_6$. Assuming that all other parameters such as the threshold and slope of the gain function are already fixed, we write the output as

$$y = y\left(x_1, x_2, x_3, w_1, w_2, w_3, w_4, w_5, w_6\right)$$

where the function $y(\cdots)$ is nonlinear because of the nonlinearity of the gain function. A learning rule for this perceptron can be derived in a similar way as for the simple linear perceptron, following the gradient descent method:

$$\Delta w_i = -\eta \frac{\partial E}{\partial w_i}$$

where $\eta > 0$ is the learning rate and $E = \frac{1}{2}(y - Y)^2$ is the error function, with Y being the

desired output. Show that this learning rule can be written as

$$\Delta w_i = \eta (Y - y) \frac{\partial y}{\partial w_i}$$
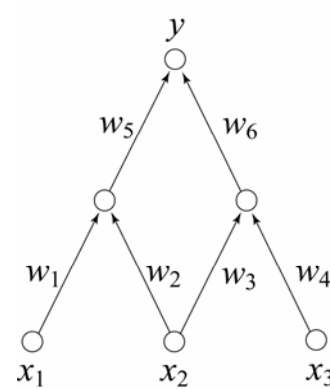
Question 13 (4 Points)

The diagram below is taken from the original research paper in which spike-time-dependent synaptic plasticity was first reported in hippocampal principal neurons. Here EPSC stands for excitatory post synaptic current, and an increase in EPSC amplitude means strengthening of the synapse. Each circle is a data point obtained after synaptic plasticity was induced by certain pre- and post-synaptic activities. Let t_1 be the time of the presynaptic spike and t_2 be the time of the postsynaptic spike. Indicate what the horizontal axis ("Spike timing") actually represents in terms of t_1 and t_2 by circling only one answer from the list below:

(1) $t_1 - t_2$

(2) $t_2 - t_1$

(3) $t_1 + t_2$

(4) t_1

(5) t_2
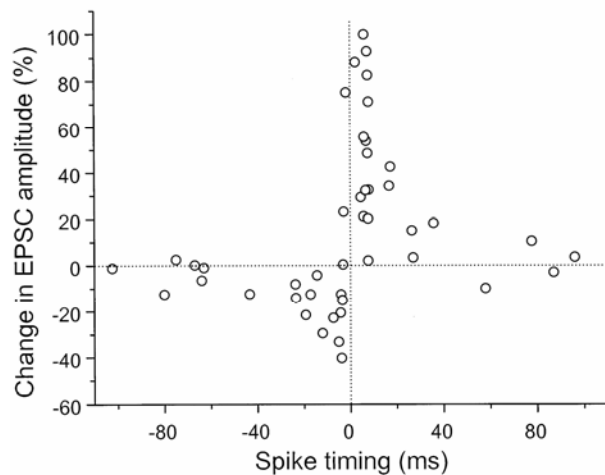
Question 14 (4 Points)

The following statements about he NMDA channels are true except for one. So circle the only one that is false.

(1) The opening of NMDA channels requires both the presence of the neurotransmitter glutamate and the depolarization in the postsynaptic membrane.

(2) NMDA channels are important for a form of synaptic plasticity that resembles a learning rule proposed by Hebb.

(3) Once opened, NMDA channels allow several types of ions to pass through except for Ca^{2+}, which fact has important consequences.

(4) NMDA channels are present in many parts of the brain, and are particularly abundant in the hippocampus, a structure important for learning and memory.

(5) In genetically altered mice with abnormal NMDA channels, an animal may no longer remember useful spatial locations.

Question 15 (4 Points)

Consider a simple Hopfield network with N neurons, whose states are updated in discrete time according to

$$s_i(t+1) = g\left(\sum_{j=1}^{N} w_{ij} s_j(t)\right)$$

where $s_j(t)$ is the state of neuron j at time t, and the gain function g is the sign function (that is, $g(x)=1$ when $x>0$ and $g(x)=-1$ when $x<0$, and $g(0)=0$). Suppose we want to store the following three activity patterns: $\mathbf{A} = (A_1, A_2, \cdots, A_N)$, $\mathbf{B} = (B_1, B_2, \cdots, B_N)$, and $\mathbf{C} = (C_1, C_2, \cdots, C_N)$, where each entry (that is, A_i, B_i, or C_i) is equal to either 1 or -1. We use the simple Hebb rule to store these patterns in the synaptic weight matrix:

$$w_{ij} = A_i A_j + B_i B_j + C_i C_j$$

Suppose $s_j(t) = A_j$ for $j = 1, 2, \cdots, N$ (this means that the state of the network at time t is the same as the stored pattern $\mathbf{A}$). Show that the state at the next time step is

$$s_i(t+1) = g\left(A_i N + B_i \sum_{j=1}^{N} B_j A_j + C_i \sum_{j=1}^{N} C_j A_j\right).$$

(Hint: $A_j^2 = 1$.)

Question 16 (4 Points)

For the same network as in the last question, suppose that pattern **A** is orthogonal both to pattern **B** and to pattern **C**; that is,

$$B \bullet A = \sum_{j=1}^{N} B_j A_j = 0$$

$$C \bullet A = \sum_{j=1}^{N} C_j A_j = 0$$

Starting from $s_i(t) = A_i$ for all neuron i, then at the next time step, which one of the following must always be true (pick only one answer):

(1) $s_i(t+1) = A_i$.
(2) $s_i(t+1) = B_i$
(3) $s_i(t+1) = C_i$
(4) $s_i(t+1) = B_i + C_i$
(5) none of the above has to be true.

Question 17 (4 Points)

Consider a long chain of neurons in which the synaptic weight from each neuron to its left neighbor is different from the synaptic weight to its right neighbor at the same distance. This synaptic connectivity is a necessary condition for which of the following phenomenon to happen (pick only one answer):

(1) Existence of at least one stable state as a point attractor
(2) Competition between multiple stable states
(3) Periodic oscillation between two states
(4) Synchronous activity of the entire network
(5) Traveling wave of activity

Question 18 (4 Points)

Which one of the following statements about recurrent networks is false (pick only one answer):

(1) A recurrent network may store multiple activity patterns as stable states, and the whole pattern can be retrieved correctly from an input that contains only partial cues.
(2) After random damage to the synaptic weights, a recurrent network may still be able to retrieve the stored memory patterns correctly.
(3) Depending on the parameters, the excitatory-inhibitory population network can approach either a stable periodic oscillation (a limit cycle) or a stationary state.
(4) In a chain of neurons where the synaptic weights between two neurons depend only on their distance in the chain, the final stable activity pattern may be a shifted version of the same shape.
(5). Depending on the synaptic weight matrix, a recurrent network may allow a Liapunov function or energy function, which guarantees that the network oscillates periodically.